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EXAMINER	
KELLY, ROBERT M	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 12/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/843,922	FUKUMURA ET AL.	
	Examiner	Art Unit	
	Robert M Kelly	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-4,6,8-11 and 16-21 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-4,6,8-11 and 16-21 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendments and arguments of 5 October 2004 have been entered.

Claims 5, 7, and 12-15 are cancelled.

Claims 1, 6, 8, 9, 11, and 16 are amended.

Claims 18-21 are newly added.

Claims 1-4, 6, 8-11, and 16-21 are presently pending and considered.

Double Patenting – old rejection

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

In light of Applicant's amendments and arguments, the rejection of Claim 16 under 35 U.S.C. 101 as claiming the same invention as that of claims 1, 2, 8, and 9 of prior U.S. Patent No. 6,723,532, filed 30 April 1998, patented 20 April 2004, is withdrawn.

Double Patenting, NonStatutory – old rejection

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 16 is provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 of copending Application No. 09/728,207. Although the conflicting claims are not identical, they are not patentably distinct from each other because Claim 16 of the instant application is drawn to any negative strand RNA virus, and Claims 1-3 of copending Application No. 09/728,207 encompass one such virus vector, Sendai virus vectors, comprising deletions of endogenous genes or insertions of exogenous genes. Therefore these claims encompass common subject matter.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

In light of Applicant's request (Applicant's response of 5 October 2004, p. 9), this rejection is held in abeyance until such time as otherwise allowable subject matter is established.

Double Patenting, NonStatutory – old rejection

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground

provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 16 is provisionally rejected under the judicially created doctrine of double patenting over claims 1-3 of copending Application No. 09/720,003. This is a provisional double patenting rejection since the conflicting claims have not yet been patented.

The subject matter claimed in the instant application is fully disclosed in the referenced copending application and would be covered by any patent granted on that copending application since the referenced copending application and the instant application are claiming common subject matter, as follows: Claim 16 of the instant application is drawn to any negative strand RNA virus. Claims 1-3 of copending Application No. 09/720,003 are drawn to the subset of negative strand RNA viruses that are sendai viruses comprising insertions, deletions, or gene inactivations that do not remove the disseminative capacity of the virus. Hence Claim 16 of the instant application encompasses all of Claims 1-3 of copending Application No. 09/720,003.

In light of Applicant's request (Applicant's response of 5 October 2004, p. 9), this rejection is held in abeyance until such time as otherwise allowable subject matter is established.

Double Patenting, NonStatutory – old rejection

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-6, 8-11, and 15-16 are provisionally rejected under the judicially created doctrine of double patenting over claims 1-6, 8-10, and 14-18 of copending Application No. 09/720,979. This is a provisional double patenting rejection since the conflicting claims have not yet been patented.

In light of Applicant's request (Applicant's response of 5 October 2004, p. 9), this rejection is held in abeyance until such time as otherwise allowable subject matter is established.

Double Patenting, NonStatutory – old rejection

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 16 is provisionally rejected under the judicially created doctrine of double patenting over claim 1 of copending Application No. 10/444,661. This is a provisional double patenting rejection since the conflicting claims have not yet been patented.

In light of Applicant's request (Applicant's response of 5 October 2004, p. 9), this rejection is held in abeyance until such time as otherwise allowable subject matter is established.

Priority

In light of Applicant's amendments and arguments of 5 October 2004, the objection to the specification for lacking a sentence stating the Application's priority is withdrawn.

Claim Rejections - 35 USC § 112 – new matter

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

In light of Applicant's amendments and arguments of 5 October 2004, the rejections of Claims 1-6, 8-11, and 15-16 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement are withdrawn.

Claim Rejections - 35 USC § 112 – written description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 9-10 remain rejected, and Claim 16 is newly rejected, for reasons necessitated by the amendments, under 35 U.S.C. 112, first paragraph, as failing to comply with the written

description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant's claims have been amended to limit the proteins capable of protecting the brain from ischemia to any protein selected from the group consisting of FGFs, NGFs, apoptosis inhibitors, HSPs, peroxidases, and neurotrophic factors.

With the limiting of such proteins to the various genera overcomes the written description requirement for proteins capable of protecting from ischemia, the rejection is maintained on the basis of neurotrophic factors.

Response to Arguments – written description

Applicant's arguments of 5 October 2004 have been fully considered but are not persuasive.

Applicant argues similar arguments with regard to each of the genera originally rejected for lacking written description. Applicant first argues that there are a number of ways to satisfy the written description requirement, including disclosure of relevant identifying characteristics, functional characteristics coupled with a correlation between structure and function, or by the combination of both of these, in which each of these must sufficiently demonstrate that the Applicant was in possession of the claimed genus (Applicant's response of 5 October 2004, pp. 11-12, paragraph bridging). Moreover, Applicant argues that the PTO guidelines note that "what constitutes a 'representative number' is an inverse function of the skill and knowledge in the art" (Id., p. 12, paragraph 2). Applicant then argues that the listing of specific species within each genera, when considered from the perspective of a high level of skill in the art, provides for

adequate written description of each genera, and, with regard to the relevant rejection, for neurotrophic factors (Id., pp. 13-14, paragraph bridging).

Applicant is correct with respect to the analysis of written description. Written description may be provided by structure (identifying characteristics), functional characteristics coupled to a structure, whether by correlative data or other, and combinations of those. Moreover, when the skill level in an art is high, the Artisan is likely to be able to determine the members of the genera more readily due to superior knowledge. However, in the instant case, Applicant has not provided common structure to distinguish the various members of the genera from each other (Official Action of 5 May 2004, p. 12, paragraph 2). Moreover, while some modicum of functional characteristics are provided (Id.), these characteristics are not linked by correlative or other data to any structure. Moreover, what functional characteristics are provided for neurotrophic factors, i.e., to protect the brain from ischemia, is also common to other genera, as Applicant's currently-amended claim recites (e.g., fibroblast growth factors and nerve growth factors and apoptosis inhibitors, and heat shock proteins and peroxidases). Hence, it is clear that no written description can be found for neurotrophic factors, even in light of the high level of skill in the art.

Claim Rejections - 35 USC § 112 – written description, necessitated by amendment

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 9 and 16 are newly rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The invention of Claims 9 and 16 encompasses any fibroblast growth factors, any nerve growth factors, any apoptosis inhibitors, any heat shock proteins, and any peroxidases.

These agents of these claims are broad in scope, being defined on the basis of their effect, and not on any specific structure. The specification broadly discloses any apoptosis-suppressing gene (p. 8, paragraph 2; p. 10, line 13); any nerve growth factor (p. 10, line 13); any heat shock protein (Id., line 14); any peroxidase (Id.); and fibroblast growth factor (Id.).

In analyzing whether the written description requirement is met for genus claims, it is first determined whether a representative number of species have been described by their complete structure. In the instant case, FGF-1, FGF-2, FGF-5, NGF, CNTF, BDNF, GDNF, p35, crmA, ILP, bcl-2, and ORP-150 have been described; however, these sequences do not contain a common structure from which to distinguish the various members of any of the aforementioned genera. The specification does not provide any disclosure as to what would have been the required structure which would allow one to distinguish the various species of the genera. Next then, it is determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics (i.e., other than nucleotide sequence), specific features and functional attributes that would distinguish different members of the claimed genus. In the instant case, the only other characteristics are the functional

characteristic common to all of the genera: capable of protecting the brain from ischemia, as well as being an apoptosis-suppressing gene, a nerve growth factor, a heat shock protein, or a peroxidase (p. 10, lines 12-25).

Such functional characteristics, however, do not allow one of skill in the art to distinguish the different members of the genera from each other.

Applicant's attention is directed to *In re Shokal*, 113 USPQ 283 (CCPA 1957), wherein it is stated:

> It appears to be well settled that a single species can rarely, if ever, afford sufficient support for a generic claim. *In re Soll*, 25 CCPA (Patents) 1309, 97 F2d 623, 38 USPQ 189; *In re Wahlforss*, 28 CCPA (Patents) 867, 117 F2d 270, 48 USPQ 397. The decisions do not however fix any definite number of species which will establish completion of a generic invention and it seems evident therefrom that such number will vary, depending on the circumstances of particular cases. Thus, in the case of small genus such as the halogens, consisting of four species, a reduction to practice of three, perhaps even two, might serve to complete the generic invention, while in the case of a genus comprising hundreds of species, a considerably larger number of reductions to practice would probably be necessary.

In conclusion, this limited information is not deemed sufficient to reasonably convey to one skilled in the art that Applicant is in possession of any apoptosis-inhibitor, any nerve growth factor, any heat shock protein, or any peroxidase, at the time the application was filed. Thus it is concluded that the written description requirement is not satisfied for the claimed genus.

Response to Arguments – written description, necessitated by amendments

Applicant's arguments of 5 October 2004 have been fully considered but are not found persuasive.

Applicant's arguments that of the argument given for "neurotrophic factors" (Supra, pp. 10-11). Applicant argues, essentially that the level of skill in the art is high, and therefore, for

each genera, enough disclosure is provided (Applicant's response of 5 October 2004, p. 12, last paragraph-p. 13, second paragraph).

Such is not persuasive for the same reasons as given for neurotrophic factors (Supra, pp. 10-11). Specifically, written description may be provided by structure (identifying characteristics), functional characteristics coupled to a structure, whether by correlative data or other, and combinations thereof. Moreover, when the skill level in an art is high, the Artisan is likely to be able to determine the members of the genera more readily due to superior knowledge. However, in the instant case, Applicant has not provided common structure to distinguish the various members of the genera from each other. Moreover, while some modicum of functional characteristics are provided, these characteristics are not linked by correlative or other data to any structure. Moreover, what functional characteristics are provided for the various genera, i.e., to protect the brain from ischemia, is also common to other genera, as Applicant's currently-amended claim recites (e.g., fibroblast growth factors and nerve growth factors and apoptosis inhibitors, and heat shock proteins and peroxidases). Hence, it is clear that no written description can be found for these genera, even in light of the high level of skill in the art.

Claim Rejections - 35 USC § 112 – enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

In light of Applicant's cancellation of Claim 3 in the response of 5 October 2004, the rejection of Claims 5 and 15 for lacking an enabling disclosure is rendered moot, and thus withdrawn.

Claims 1-5, 8-11, and 16 remain rejected and Claims 17-21 are newly rejected as necessitated by the amendments, for reasons of record, under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

(i) a method of delivery of a nucleic acid sequence to mammalian nerve cells *in vitro* comprising a step of contacting such cells with a Sendai viral vector comprising the nucleic acid sequence to be delivered, which nucleic acid sequence is inserted between the R1 and R2 locuses of the Sendai viral vector,

(ii) a method of delivering a nucleic acid sequence encoding a protein to rodent nerve cells *in vivo* comprising the direct administration of a Sendai viral vector comprising such sequences between the R1 and R2 locuses of the vector to the nerve cells, by direct injection, wherein the transgene is expressed, thereby causing expression of the transgene, and

(iii) vectors commensurate in structure with the vectors of (i) and (ii).

does not reasonably provide enablement for any method of administration, any ex vivo method, or the treatment of any mammal. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Applicant's amended claims are to "contact the nerve cells directly" with the vector, which is now a sendai virus with the foreign gene placed between R1 and R2 loci (Claim 1). Claims 6, 8-9, and 11 now depend from Claim 1, limiting the proteins and their transient

expression. Claim 16 is now independent, and drawn to the vector, but still comprises a foreign gene capable of protecting the brain from ischemia, and is therefore still read in the context of the specification as requiring enablement for *in vivo* and *ex vivo* treatment of mammals. Claims 17-18 and 21 encompass specific foreign genes. Claims 19-20 depend from Claim 2 and are drawn to intraventricular administration and intraspinal administration, respectively.

It is noted that Applicant's newly amended claim 1 requires the nerve cells to be contacted directly with the vector, however, such is not equivalent to direct administration, as required by the examiner. The claim is currently read by the examiner to encompass any method which eventually leads to such nerve cells being contacted by the vector. As such, these methods must be reasonably predictive of such treatment.

Response to Arguments – Enablement

Applicant's arguments of 5 October 2004 have been fully considered but are not found fully persuasive.

Applicant argues that the amendments overcome the rejection with respect to the vector and location of the foreign gene are overcome (Applicant's response of 5 October 2004, p. 15, paragraph 3).

Such is persuasive, and Applicant's should note the change in the scope of enablement; however the balance of Applicant's are not persuasive, as reviewed below.

Applicant argues that "several of the references cited" either do not reflect the state of the art and/or are not pertinent to the claimed invention, or both; specifically, the references fail to challenge the utility and operability of Sendai viral vectors (Applicant's argument of 5 October 2004, pp. 15-16, paragraph bridging).

Applicant's argument is not persuasive. Utility arguments are not addressed in enablement; such argument is properly addressed with respect to rejections under 35 USC 101 for utility. Also, Applicant has failed to address how Sendai vectors are different and not subject to the reasoning provided by any reference.

Applicant argues that Nakanishi supports Applicant's enablement because the fusogenic liposomes are likely targeted by SeV envelope proteins, and hence, that Nakanishi supports Applicant's enablement.

Such is not persuasive. Nakanishi's fusogenic liposomes are not the same as Applicant's vectors, and these fusogenic liposomes are less efficient at targeting than Sendai vectors. Therefore, the Artisan could not reasonably predict from Nakanishi's fusogenic liposome results that any Sendai vector would act similarly, as far as targeting is concerned (Official Action of 5 May 2004, p. 21, paragraph 2).

Applicant argues, submitting two abstracts and one article published by Nakanishi's group, that fusogenic liposomes are an efficient tool for delivery of CTL vaccines, versatile and effective for stimulating antigen responses, and potentially useful delivery vehicles for gene therapy. Hence, Applicant asserts, Nakanishi's work supports Applicant's vectors.

Such is not persuasive. With regard to Nakanishi, et al. (2000) Eur. J. Immunology, 30(6): 1740-47 was submitted as only an abstract, and it is unknown whether these results are *in vivo* or *in vitro*. Second, the delivery of proteins to the MHC pathways does not require the targeting that gene therapy would require; it simply requires the delivery of such proteins to any cell. Third, the fusogenic liposomes are not Applicant's Sendai virus vectors, and are therefore not predictive of Applicant's Sendai virus vectors as far as targeting is concerned. (E.g., Official

Action of 5 May 2004, p. 21, paragraph 2). With regard to Kunisawa, et al. (2001) J. Immunol., 167(3): 1406-12, such fusogenic liposomes delivery antigens and not genes, and are administered by nasal administration for stimulating immune response, not for treating brain ischemia. Third, the fusogenic liposomes are not Applicant's Sendai virus vectors, and are therefore not predictive of Applicant's Sendai virus vectors as far as targeting is concerned. (E.g., Official Action of 5 May 2004, p. 21, paragraph 2). With regard to Kondoh, et al. (2000) Biol. Pharm. Bull., 23(8): 1011-13, only the abstract was attached, and it is likely that these results were obtained *in vitro,* and hence do not overcome the targeting problems of fusogenic liposomes. Second, these results do not reflect any treatment of ischemia of any kind, much less the brain. Third, the fusogenic liposomes are not Applicant's Sendai virus vectors, and are therefore not predictive of Applicant's Sendai virus vectors as far as targeting is concerned. (E.g., Official Action of 5 May 2004, p. 21, paragraph 2). Lastly, it is noted that Kondoh does not predict the use of such vectors, but that these vectors are **potentially** useful in therapy (ABSTRACT). Hence, even Kondoh does not find their use reasonably predictable.

Applicant argues that Yonemitu is mentioned with concerns of the practicalities to cardiovascular disease and the complexity of the disease, and hence this does not challenge the utility of such vectors in gene therapy to nerve tissues (Applicant's response of 5 October 2004, p. 17, paragraph 1).

Such is not found persuasive. Utility arguments are addressed with regard to rejections under 35 USC 101, for lacking utility. Also, Yonemitsu's arguments that lead the Artisan do doubt the reasonable predictability of such vectors for other diseases reflects the same with Applicant's core interest: protecting the brain from ischemia. Such is conveyed when one

considers the context in which Yonemitsu is presented (Official Action of 5 May 2004, pp. 20-21). Essentially, Yonemitsu discusses the targeting problem, which is common to Applicant's gene therapy (Id.). Moreover, in the case of a known diseases that may be treated with VEGF, many unknown factors need to be resolved with regard to the actions of the factor being used to treat the disease before it becomes reasonably predictable (Id.). Hence, Applicant's less well defined disease, brain ischemia, is even less predictable for targeting problems as well as the actions of the individual factors which are be expressed in the tissues once the targeting problem is overcome.

Applicant argues that Yonemitsu notes that new Sendai viral vectors appear to be superior to previous vectors, demonstrating superior gene transfer efficiency in several organs. Therefore, Applicant argues that Yonemitsu is completely enabling for Applicant's invention (Applicant's response of 5 October 2004, p. 17, paragraph 1).

Such is not persuasive. At the outset, just because one vector is superior in some way(s) to another vector that is found inadequate, does not mean that the first vector is completely enabled. Such argument fails to realize that even though the vector may be better in some way(s), it may still fail in other ways. Moreover, being superior does not mean being perfectly predictable. Second, Applicant notes that Yonemitsu "offers new possibilities", but it is noted that Applicant does not state that Yonemitsu predicts the use in any particular gene therapy, much less for treating brain ischemia. Lastly, Yonemitsu also recognizes that problems still exist that need to be addressed before gene therapy protocols for *inter alia*, Sendai vectors, is reasonably predictable (p. 266). (Official Action of 5 May 2004, pp. 20-21, paragraph bridging).

Applicant broadly argues that each of the references to Verma, Eck, Gorecki, and Deonarain, in the nature of the invention do not, individually, apply to Sendai viral vectors (Applicant's response of 5 October 2004, pp. 17-19). Similarly, Applicant argues that the references are dated and do not reflect the current state of the art (Id.).

Such is not persuasive. Piecemeal arguments against each article is not sufficient to overcome the nature of the invention. The Articles together clearly tell a story of a lack of reasonable predictability that must be overcome to allow the Artisan to practice the full scope of Applicant's claims without having to perform undue experimentation. In response to applicant's argument based upon the age of the references, contentions that the references are old are not impressive absent a showing that the art tried and failed to solve the same problem notwithstanding its presumed knowledge of the references. See *In re Wright*, 569 F.2d 1124, 193 USPQ 332 (CCPA 1977).

Applicants argue that the information set forth in the specification overcomes the unpredictable nature of the art set forth in the rejection, with regard to the references to Verma, Eck, Gorecki, and Deonarain (Id.).

Such is not persuasive. The scope of the enablement is the scope that is overcome when considering the lack of predictability in the art, the breadth of the claimed subject matter, and the amount of experimentation the Artisan would have to perform to overcome the lack of predictability in the art. Applicant's broad argument that the disclosure of Applicant overcomes such lack of reasonable predictability in the art fails to even address one specific issue addressed.

Applicant argues that Crystal and Gura are dated and do not reflect the state of the art at the time of invention by Applicant (Applicant's arguments of 5 October 2004, p. 19, paragraph 3).

Such is not persuasive. In response to applicant's argument based upon the age of the references, contentions that the references are old are not impressive absent a showing that the art tried and failed to solve the same problem notwithstanding its presumed knowledge of the references. See *In re Wright*, 569 F.2d 1124, 193 USPQ 332 (CCPA 1977).

Applicant argues that Crystal expressly states that "enough information has been gained from clinical trials to allow the conclusion that human gene transfer is feasible, can evoke clinical responses that are relevant to human disease" and "adverse events have been uncommon and have been related to the gene delivery strategies (i.e., the delivery system)" while "human gene transfer still faces significant hurdles before it becomes and established therapeutic strategy", "its accomplishments to date are impressive and the logical of the potential usefulness of the clinical paradigm continues to be compelling". (Applicant's argument of 5 October 2004, p. 19, paragraph 3).

Such is not persuasive. Crystal is simply evincing an optimistic outlook, recognizing the problems with gene delivery strategies (which include Applicant's vectors) and stating that the future is bright, but not that it is reasonably predictable, such that the artisan would not have to perform undue experimentation to practice broad subject matter. Thus, from Crystal, the Artisan could only conclude that successful results were peculiar to that particular animal, and would not extrapolate to other animals (Official Action of 5 May 2004, p. 18, paragraph 1).

Applicant argues broadly that the animal data presented in two models in the experimental results reported in the specification provides enough information for the Artisan not to doubt the feasibility of the methods and vectors in other mammals than rodents, arguing that the *in vivo* results outweight the unpredictability in the art (Applicant's response of 5 October 2004, p. 20, paragraph 1).

Such is not persuasive. The vast majority of the art provides the same rationale and supporting reasons for a lack of unpredictability that must be overcome for the Artisan to avoid undue experimentation in practicing the breadth of Applicant's claims. Applicant's results are simply not enough to overcome the overwhelming opinion of the art as to a lack of reasonable predictability, for, *inter alia*, the vectors, route of administration, and across animal species (e.g., Official Action of 5 May 2004, p. 24, paragraph 2).

Applicant argues that the expression of two reporter genes and beta-glucoronidase directly correlate to therapy and thus overcomes the usefulness of Applicant's invention to treat neurodegenerative diseases, including Parkinson's disease, ischemia, and the like (Applicant's response of 5 October 2004, p. 20, paragraph 2).

Such is not persuasive. Applicant is reminded that usefulness is directed to arguments under 35 USC 101 for lacking utility. Moreover, given the overwhelming opinion of the Art as to a lack of reasonable predictability, for, *inter alia*, the vectors, route of administration, and across animal species (e.g., Official Action of 5 May 2004, p. 24, paragraph 2). Lastly, Applicant's administration to animals is limited to direct administration to the brain by stereotactic injection, and Applicant's claims encompass any method of obtaining direct contact.

It is argued that it is not reasonably predictable that any route of administration will yield direct contact between the vector and any neural cell (e.g, Id., paragraphs 1-2).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

In light of Applicant's amendments and arguments of 5 October 2004, the rejection of Claim 16 under 35 U.S.C. 102(b) as being anticipated by Hasan, et al. (1997) J. Gen. Virology, 78: 2813-20, is withdrawn.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

In light of Applicant's amendments and arguments of 5 October 2004, the rejection of Claim 16 under 35 U.S.C. 102(e) as being anticipated by Patent Application Publication No.: US

2002/0100066 to Nagai, et al., filed 13 September 2001, published 25 July 2002, and claiming priority to Japanese application number 7/308315, filed 31 October 1995, is withdrawn.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

In light of Applicant's amendments and arguments of 5 October 2004, the rejection of Claim 16 under 35 U.S.C. 102(e) as being anticipated by Patent Application Publication No.: US 2002/0098576 to Nagai, et al., filed 1 December 2000, Published 25 July 2002, and claiming priority to Japanese Application 7/285417, filed 1 November 1995, is withdrawn.

Claims free of the Prior Art of Record

The claims are free of the prior art of record.

CONCLUSION

No Claim is allowed for reasons of record or for reasons necessitated by the amendments.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert M Kelly whose telephone number is (571) 272-0729. The examiner can normally be reached on M-F, 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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